

AMENDMENT

In the Claims:

Please amend the claims as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application:

1.-33. (Canceled)

34. (Previously Presented) A hepatitis C virus (HCV) vaccine comprising at least two epitopes, each from a different hotspot epitope, wherein a hotspot epitope is defined as an epitope containing at least one of the following peptides:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
GYKVLVLNPSVAAT (SEQ ID NO:60),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132; SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),,
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDNRSELSPLLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93),
LINTNGSWHINRTALNCNDSL (SEQ ID NO:84),
TTILGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDLCGSV (SEQ ID NO:5),

GVLFGLAYFSMVGNW (SEQ ID NO:56),
VVCCSMSYTWGTGALITPC (SEQ ID NO:144),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126).

35. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising at least three epitopes, each from a different hotspot epitope.

36-38. (Canceled)

39. (Previously Presented) The HCV vaccine of claim 34, wherein the epitopes are at least two of:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
KFPGGGQIVGGVYLLPRRGPRL (SEQ ID NO:72), YLLPRRGPRL (SEQ ID NO:146),
LPRRGPRL (SEQ ID NO:86), GPRLGVRAT (SEQ ID NO:50), RLGVRATRK (SEQ ID
NO:103), GYKVLVLNPSVAAT (SEQ ID NO:60), AYAAQGYKVL (SEQ ID NO:9),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14); DLMGYIPAV (SEQ ID NO:19),
GYIPLVGAPL (SEQ ID NO:59), DLMGYIPLVGAPL (SEQ ID NO:25), CINGVCWTV
(SEQ ID NO:17), GEVQVVSTATQSFLAT (SEQ ID NO:47),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63), MWNFISGIQYLAGLSTLPGN
(SEQ ID NO:94), NFISGIQYLAGLSTLPGNPA (SEQ ID NO:97), QYLAGLSTL (SEQ
ID NO:101), HMWNFISGI (SEQ ID NO:61),
VDYPYRLWHYPCTVNFTIFKVRMYVGGVEHRL (SEQ ID NO:132),
DYPYRLWHYPCTVNFTIFKI (SEQ ID NO:35), DYPYRLWHYPCTVNFTIFKV (SEQ
ID NO:36), VDYPYRLWHYPCTVNYTIFKIRMYVGGVEHRL (SEQ ID NO:135),
DYPYRLWHYPCTVNYTIFKI (SEQ ID NO:38), DYPYRLWHY (SEQ ID NO:33),
TVNYTIFKI (SEQ ID NO:129), TINYTIFK (SEQ ID NO:120), TVNFTIFKV (SEQ ID
NO:127), HYPCTVNYTI (SEQ ID NO:67), HYPCTVNFTI (SEQ ID NO:66),
RMYVGGVEHR (SEQ ID NO:106), AAWYELTPAETTVRLR (SEQ ID NO:4),
TPAETTVRL (SEQ ID NO:121), GWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:57),
TAYSQQTRGLLGCIV (SEQ ID NO:116), TAYSQQTRGLLG (SEQ ID NO:115),

GQGWRLAPITAYSQ (SEQ ID NO:52), RLLAPITAY (SEQ ID NO:105),
 GQGWRLAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
 GQGWRLAPITAYSQQTRGLLG (SEQ ID NO:53), AYSQQTRGLL (SEQ ID NO:16),
 AYSQQTRGL (SEQ ID NO:15), IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID
 NO:70), ILAGYGAGV (SEQ ID NO:71), VAGALVAFK (SEQ ID NO:131),
 GYGAGVAGAL (SEQ ID NO:58), VVCCSMSYTWGTGALITPC (SEQ ID NO:144),
 SMSYTWGTGALITP (SEQ ID NO:112), SMSYTWGTGAL (SEQ ID NO:111),
 SYTWGTGALI (SEQ ID NO:114), FTDNSSPPAVPQTFQV (SEQ ID NO:46),
 LEDRDRSELSPLLLSTTEW (SEQ ID NO:80), LEDRDRSELSPLLLST (SEQ ID
 NO:79), RSELSPLLL (SEQ ID NO:108), ELSPLLLST (SEQ ID NO:39),
 DRDRSELSPL (SEQ ID NO:32), LEDRDRSEL (SEQ ID NO:78), LEDRDRSEL (SEQ
 ID NO:78), YLVAYQATVCARAQAPPSWD (SEQ ID NO:149), YLVAYQATV (SEQ
 ID NO:148), MSTNPKPQRKTKRNTNR (SEQ ID NO:93), PQRKTKRNTNR (SEQ ID
 NO:99), QRKTKRNTN (SEQ ID NO:100), RKTKRNTNR (SEQ ID NO:102),
 MSTNPKPQR (SEQ ID NO:92), MSTNPKPQK (SEQ ID NO:91),
 INTNGSWHINRTALNCNDSL (SEQ ID NO:84), NGSWHINRTALNCNDSL (SEQ ID
 NO:98), LINTNGSWHI (SEQ ID NO:82), RTALNCNDSL (SEQ ID NO:109),
 LINTNGSWHINRTALN (SEQ ID NO:83), SWHINRTALN (SEQ ID NO:113),
 TTILGIGTVLDQAET (SEQ ID NO:125), TTILGIGTV (SEQ ID NO:124), TILGIGTVL
 (SEQ ID NO:119), FDSSVLCECYDAGAAWYE (SEQ ID NO:40; SEQ ID NO:44),
 FDSSVLCECYDAGCA (SEQ ID NO:45), VLCECYDAGA (SEQ ID NO:142),
 VVLCECYDAGAAWYE (SEQ ID NO:145), ARLIVFPDLGVRVCEKMALY (SEQ ID
 NO:8), ARLIVFPDL (SEQ ID NO:7), RLIVFPDLGV (SEQ ID NO:104),
 RVCEKMALY (SEQ ID NO:110), AFCSAMYVGDL CGSV (SEQ ID NO:5),
 GVLFGLAYFSMVGNW (SEQ ID NO:56), TRVPYFVRAQGLIRA (SEQ ID NO:123),
 TTLLFNILGGWVAAQ (SEQ ID NO:126), LLFNILGGWV (SEQ ID NO:85).

40. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least three of the following hotspot epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
 AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
 DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),

GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49), and
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

41. (Canceled)

42. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least two of the following hotspot epitopes:

VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMVVGVEHRL (SEQ ID NO:132; SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRL LAPITAYSQQTRGLLGCI V (SEQ ID NO:54),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDRDRSELSPLLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93) and
LINTNGSWHINRTALNCNDSL (SEQ ID NO:84).

43-44. (Canceled)

45. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least two of the following hotspot epitopes:

TTILGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDL CGSV (SEQ ID NO:5),
GVLFGLAYFSMVGNW (SEQ ID NO:56),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126).

46-47. (Canceled)

48. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising at least two of the following epitopes:

KFPGGGQIVGGVYLLPRRGVRLGVRATRK (SEQ ID NO:73),
DLMGYIPAV (SEQ ID NO:19),
LEDNRSELSPLLLSTTEW (SEQ ID NO:80),
DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),
GYKVLVLNPSVAAT (SEQ ID NO:60),
CINGVCWTV (SEQ ID NO:17),
AAWYELTPAETTVRLR (SEQ ID NO:4),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
TAYSQQTRGLLG (SEQ ID NO:115),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and
SMSYTWTGALITP (SEQ ID NO:112).

49-53. (Canceled)

54. (Previously Presented) The HCV vaccine of claim 48, further defined as comprising at least two of the following epitopes:

KFPGGGQIVGGVYLLPRRGVRLGVRATRK (SEQ ID NO:73),
DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),
AAWYELTPAETTVRLR (SEQ ID NO:4),
TAYSQQTRGLLG (SEQ ID NO:115),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and
SMSYTWTGALITP (SEQ ID NO:112).

55-57. (Canceled)

58. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGVRLGVRATRK (SEQ ID NO:73).

59. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope DLMGYIPAV (SEQ ID NO:19).

60. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope CINGVCWTV (SEQ ID NO:17).

61. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

62. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope GYKVLVLNPSVAAT (SEQ ID NO:60).

63. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising the epitope VVCCSMSYTWGTALITPC (SEQ ID NO:144).

64. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising any two of the epitopes:

GYKVLVLNPSVAAT (SEQ ID NO:60),

CINGVCWTV (SEQ ID NO:17), and

HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

65. (Previously Presented) The vaccine of claim 64, further defined as comprising all three of the epitopes.

66. (Previously Presented) The vaccine of claim 65, further defined as comprising the epitope DLMGYIPAV (SEQ ID NO:19).

67. (Previously Presented) The vaccine of claim 65, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGPR (SEQ ID NO:72).

68. (Previously Presented) The vaccine of claim 65, further defined as comprising the epitopes DLMGYIPAV (SEQ ID NO:19) and KFPGGGQIVGGVYLLPRRGPR (SEQ ID NO:72).

69. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising a peptide ("Peptide A") comprising a sequence $R_1\text{-XZXX}_N\text{XZX-R}_2$, (SEQ ID NOS:152-156, where N is 3-7, respectively) wherein:

N is a whole number between 3 and 7;

X is a positively charged natural and/or non-natural amino acid residue;

Z is an amino acid residue selected from the group consisting of L, V, I, F and/or W;

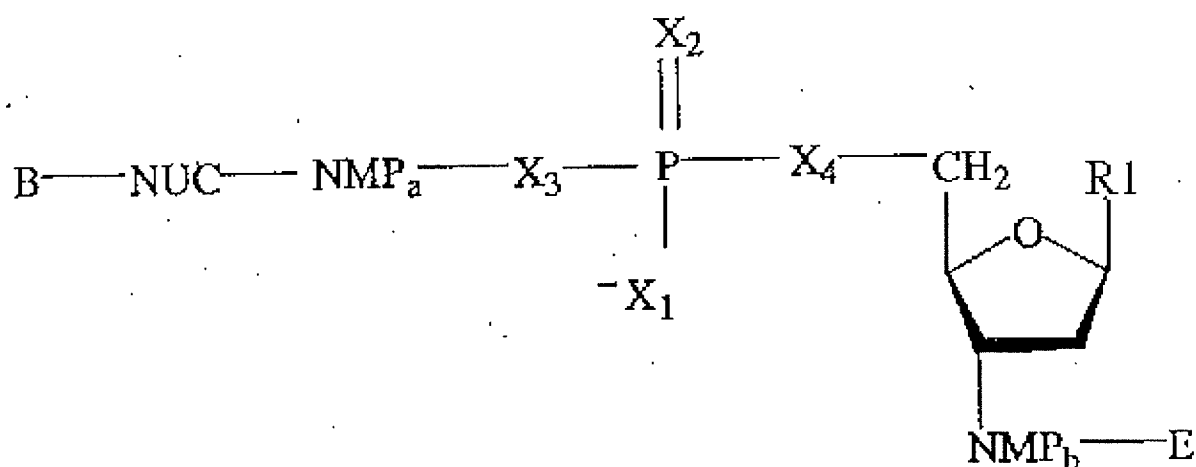
and R_1 and R_2 are independently: -H, -NH₂, -COCH₃, -COH, a peptide with up to 20 amino acid residues or a peptide reactive group, or a peptide linker with or without a peptide; and

$X\text{-R}_2$ may be an amide, ester or thioester of the C-terminal amino acid residue of the peptide.

70. (Canceled)

71. (Previously Presented) The HCV vaccine of claim 69, wherein the sequence of Peptide A is KLKL₅KLK (SEQ ID NO:75).

72. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising an immunostimulatory oligodeoxynucleic acid molecule (ODN) having the structure according to the formula (I):



wherein

R1 is selected from hypoxanthine and uracil;

any X is O or S;

any NMP is a 2' deoxynucleoside monophosphate or monothiophosphate, further defined as: deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxyuridine-, deoxythymidine-, 2-methyl-deoxyinosine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine-monophosphate or -monothiophosphate,

NUC is a 2' deoxynucleoside, further defined as deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxyinosine-, deoxythymidine-, 2-methyl-deoxyuridine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine;

a and b are integers from 0 to 100 with the proviso that $a + b$ is between 4 and 150; and

B and E are common groups for 5' or 3' ends of nucleic acid molecules ("I-/U-ODN").

73. (Previously Presented) The HCV vaccine of claim 72, wherein said I-/U-ODN is oligo d(IC)₁₃.

74. (Canceled)

75. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising a polycationic peptide.

76. (Previously Presented) The HCV vaccine of claim 34, further defined as comprising an oligodeoxynucleotide containing a CpG-motif.

77-84. (Canceled)